Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS) — revised report of an EFNS task force.

Bibliographic Source(s)

EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis, Andersen PM, Abrahams S, Borasio GD, de Carvalho M, Chio A, Van Damme P, Hardiman O, Kollewe K, Morrison KE, Petri S, Pradat PF, Silani V, Tomik B, Wasner M, Weber M. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS) -- revised report of an EFNS task force. Eur J Neurol. 2012 Mar;19(3):360-75. [186 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Andersen PM, Borasio GD, Dengler R, Hardiman O, Kollewe K, Leigh PN, Pradat PF, Silani V, Tomik B, EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis. EFNS task force on management of amyotrophic lateral sclerosis: guidelines for diagnosing and clinical care of patients and relatives. Eur J Neurol 2005 Dec;12(12):921-38.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

The levels of evidence (class I-IV) supporting the recommendations and ratings of recommendations (A-C, GCPP) are defined at the end of the

"Major Recommendations" field.

Diagnosing Amyotrophic Lateral Sclerosis (ALS)

1. The diagnosis should be pursued as early as possible. Patients in whom ALS is suspected should be referred with high priority to an experienced neurologist (GCPP).
2. All suspected new cases should undergo prompt detailed clinical and paraclinical examinations (see Tables 1 and 2 in the original guideline document) (GCPP).
3. In some cases, additional investigations may be needed (see Table 2 in the original guideline document).
4. Repetition of the investigations may be required if initial tests are equivocal (GCPP).
5. Review of the diagnosis is advisable if there is no evidence of typical progression or the patient develops atypical features (see Table 1 in the original guideline document) (GCPP).

Breaking the News: Communicating the Diagnosis

1. The diagnosis should be communicated by a consultant with a good knowledge of the patient (GCPP).
2. The physician should start the consultation by asking what the patient already knows or suspects (GCPP).
3. The diagnosis should be given in person, ensuring enough time for discussion (suggest at least 45–60 min). Provide printed materials about the disease, about support and advocacy organizations and informative websites. A copy letter summarising the discussion can be helpful for patients and carers (GCPP).
4. Assure patients that they will not be 'abandoned' by healthcare services and will be supported by a professional ALS care team (where available), with regular follow-up visits to a neurologist. Make arrangements for a first follow-up visit, ideally within 2–4 weeks (GCPP).
5. Avoid the following: withholding the diagnosis, providing insufficient information, imposing unwanted information, delivering information callously, taking away or not providing hope (GCPP).

See also Table 5 in the original guideline document for detailed recommendations on how a physician should tell patients that they have ALS.

Multidisciplinary Care

1. Multidisciplinary care should be available for people affected by ALS. Attendance at multidisciplinary clinics may extend survival, decrease medical complications (Level B), and improve quality of life (Level C).
2. The following specialists should be part of or readily available to the multidisciplinary clinic team: neurologist, respiratory physician, gastroenterologist, rehabilitation medicine physician, social counsellor, occupational therapist, speech therapist, respiratory therapist, specialized nurse, physical therapist, dietitian, psychologist, dentist, and palliative care physician (GCPP).
3. Patients should generally be reviewed every 2–3 months, although they may require more frequent review in the months following diagnosis or in the later stages of disease, and less frequent review if their disease is progressing slowly. The patient support team should maintain regular contact with the patient and relatives between visits (GCPP).
4. Ideally, the patient should be followed by the same neurologist liaising closely with the patient's primary care physician (family general practitioner) (GCPP).
5. Effective channels of communication and co-ordination are essential between the hospital-based multidisciplinary clinic team, the primary healthcare sector, the palliative care team, and community services (GCPP).

ALS Caregivers and Burden of Care

1. Caregivers should be acknowledged in their double role in the disease process: they are the most important resource for the patient, yet they are affected themselves, and their own needs as carers need to be addressed (GCPP).
2. Ideally, caregivers should be involved from the time of diagnosis, whilst preserving patients' autonomy (GCPP).
3. Carers' own health needs should be considered. Physical, psychological, and spiritual support should be provided when needed (GCPP).
4. Maintaining communication between patients and caregivers is important (GCPP).
5. The likelihood of a peaceful death process should be communicated to patients and their caregivers/relatives (GCPP).
6. Bereavement counselling and support should be offered to all caregivers (GCPP).

Neuroprotective Treatment/Disease-Modifying Treatment

1. Patients with ALS should be offered treatment with riluzole 50 mg twice daily (Level A).
2. Treatment should be initiated as early as possible after diagnosis (GCPP). Realistic expectations for treatment effects and potential side effects should be discussed with the patient and caregivers (GCPP).
3. Patients with progressive muscular atrophy, primary lateral sclerosis, or hereditary spastic paraplegia should as rule not be treated with

riluzole (GCPP).
4. Irrespective of familial disposition, all patients with a symptomatic progressive motor neuron disease (MND) and carrying a *SOD1* gene mutation should be offered treatment with riluzole (GCPP).
5. Currently, there is insufficient evidence to recommend treatment with vitamins, testosterone, antioxidants such as co-enzyme Q-10 and gingko biloba, intravenous immunoglobulin therapy, cyclosporin, interferons, Copaxone, KDI tripeptide, neurotrophic factors (including brain-derived neurotrophic factor [BDNF], insulin-like growth factor-1 [IGF-1], and mecasermin rinfabate), ceftriaxone, creatine, gabapentin, minocycline, stem cells, or lithium (GCPP).

Symptomatic Treatment

Sialorrhoea

Treat sialorrhoea in ALS with amitriptyline, oral or transdermal hyoscine, or sublingual atropine drops (GCPP).

1. In patients with refractory sialorrhoea, botulinum toxin injections into the parotid and/or submandibular gland are effective and generally well tolerated (Level B for botulinum toxin type B, level C for type A toxin).
2. Irradiation of the salivary glands may be tried when pharmacological treatment fails (GCPP).
3. Surgical interventions are not recommended (GCPP).

Bronchial Secretions

1. A mucolytic including *N*-acetylcysteine, 200–400 mg three times daily, may be beneficial (GCPP).
2. Beta-receptor antagonists and a nebulizer with saline and/or an anticholinergic bronchodilator and/or a mucolytic and/or furosemide may be used in combination. Mucolytics should only be used if sufficient cough flow is present (GCPP).
3. The patient and carer should be taught the technique of assisting expiratory movements using a manual-assisted cough (can also be performed by a physical therapist) (GCPP).
4. The use of a mechanical insufflator–exsufflator may be helpful, particularly in the setting of an acute respiratory infection (GCPP).
5. A portable home suction device and a room humidifier may be of use (GCPP).

Pseudobulbar Emotional Lability

1. Inform the patient and relatives that emotional lability is not a sign of an additional mood disorder but is because of the effects of ALS on the brain (GCPP).
2. Troublesome emotional lability should be treated (GCPP). Antidepressants such as amitriptyline (in particular in patients with drooling), fluvoxamine, and citalopram are usually sufficient (Level C).
3. A combination of dextromethorphan and quinidine has been shown to be effective (Level A).

Cramps

1. Levetiracetam may be tried. If unsuccessful or side effects, quinine sulphate (200 mg twice daily) may be of benefit (GCPP).
2. Physiotherapy, physical exercise, and/or hydrotherapy may be helpful (GCPP).

Spasticity

1. Regular physical therapy can help relieve significant spasticity (GCPP).
2. Antispastic drugs such as baclofen and tizanidine may be tried (GCPP).
3. If spasticity is severe despite oral medications, intrathecal baclofen may be helpful (GCPP).
4. Hydrotherapy with exercises in warm pools (32–34ºC) and cryotherapy may be considered (GCPP).

Depression and Anxiety

1. Treat depression in ALS with an appropriate antidepressant, for example amitriptyline, a selective serotonin reuptake inhibitor (SSRI), or mirtazapine. SSRI may be preferably in elderly or cognitively impaired patients (GCPP).
2. Treat anxiety with bupropion or benzodiazepines such as diazepam tablets or suppositories, Temesta tablets 0.5 mg two or three times daily, or sublingual lorazepam (GCPP).

Insomnia and Fatigue

1. Treat insomnia with amitriptyline, mirtazapine or appropriate hypnotics (e.g., zolpidem) (GCPP).
2. For debilitating fatigue, modafinil may be considered (Level A).

Venous Thrombosis

1. Deep venous thrombosis (DVT) should be treated with anticoagulants (GCPP).
2. The optimum management of risk factors for venous thrombosis should be pursued. Physiotherapy, limb elevation, and compression stockings are recommended (GCPP).
3. There is currently insufficient evidence to recommend prophylactic medical treatment with anticoagulants.

Unproven Therapies

1. Before cellular therapies become a reality, a more thorough preclinical evaluation and elucidation of several open questions is mandatory (GCPP).
2. No well-designed clinical trials testing cellular therapies have as yet been completed demonstrating safety and clinical efficacy supported by pathological evidence in a sufficient number of patients.
3. Patients with ALS should be carefully informed about existing reliable data related to cell therapies. All current treatments with cell transplantation are purely experimental, and there is no proven effect on disease outcome. If they decide to undergo transplantation, thorough examination before and after the stem cell treatment should be performed and documented to improve the knowledge of benefits and/or side effects (GCPP).
4. Accurate and unbiased information related to cell therapies and other unproven/alternative therapies needs to be delivered to the patient community (GCPP).
5. All procedures involving the injection and transplantation of stem cells to a patient with ALS should be considered experimental and should be approved by a medical research ethical review board and performed in full accordance with the Declaration of Helsinki (GCPP).

Genetic Testing and Counselling

1. In all patients with suspected ALS, progressive muscular atrophy, primary lateral sclerosis, or frontotemporal dementia, a detailed medical history of the patient, siblings, parents, and grandparents and their siblings should be obtained to potentially disclose a familial disease with reduced disease penetrance (GCPP).
2. Clinical deoxyribonucleic acid (DNA) analysis for gene mutations should only be performed in cases with a known family history of ALS, and in sporadic ALS cases with the characteristic phenotype of the recessive D90A mutation (GCPP).
3. Clinical DNA analysis for gene mutations should *not* be performed in cases with sporadic ALS with a typical classical ALS phenotype (GCPP).
4. In familial or sporadic cases where the diagnosis is uncertain, SMN, androgen receptor, or *TARDBP*, *FUS*, *ANG*, or *SOD1* DNA analysis may accelerate the diagnostic process (GCPP).
5. Before blood is drawn for DNA analysis, the patient should receive genetic counselling. Give the patient time for consideration. DNA analysis should be performed only with the patient's informed consent (GCPP).
6. Presymptomatic genetic testing should only be performed in first-degree adult blood relatives of patients with a known gene mutation. Testing should only be performed on a strictly voluntary basis as outlined (see Table 7 in the original guideline document) and should follow accepted ethical principles (GCPP).
7. Results of DNA analysis performed on patients and their relatives as part of a research project should not be used in clinical practice or disclosed to unaffected relatives. The research results should be kept in a separate file and not in the patient's standard medical chart (GCPP).

Respiratory Management in Patients with ALS

1. Symptoms or signs of respiratory insufficiency (including symptoms of nocturnal hypoventilation) should be checked at each visit (GCPP).
2. Forced vital capacity and vital capacity are the most available and practical tests for the regular monitoring of respiratory function (GCPP).
3. Sniff nasal pressure (SNP) may be used for monitoring, particularly in bulbar patients with weak lips (GCPP).
4. Percutaneous nocturnal oximetry is recommended as a screening test and for monitoring respiratory function (GCPP).
5. Symptoms or signs of respiratory insufficiency should prompt discussions with the patient and caregivers about treatment options and the terminal phase. Early discussions are needed to allow advance planning and directives (GCPP).
6. Non-invasive positive pressure ventilation (NIPPV) should be considered in preference to invasive mechanical ventilation (IMV) in patients with symptoms or signs of respiratory insufficiency (GCPP).
7. NIPPV can prolong survival for many months (Level A) and may improve the patient's quality of life (Level C).
8. Active management of secretions and provision of cough-assist devices can increase the effectiveness of assisted ventilation in ALS (GCPP).
9. IMV has a major impact upon caregivers and should be initiated only after informed discussion (GCPP).

10. Unplanned (emergency) IMV should be avoided through an early discussion of end-of-life issues, coordination with palliative care teams. and appropriate advance directives (GCPP).
11. Oxygen therapy alone should be avoided as it may exacerbate carbon dioxide retention and oral dryness. Use oxygen only if symptomatic hypoxia is present (GCPP).
12. The medical treatment of intermittent dyspnoea should involve:
    a. For short dyspnoeic bouts: relieve anxiety and give lorazepam 0.5–2.5 mg sublingually.
    b. For longer phases of dyspnoea (>30 min): give morphine 2.5 mg orally or subcutaneously (s.c.) (GCPP)
13. For the medical treatment of chronic dyspnoea, start with morphine 2.5 mg orally four to six times daily. For severe dyspnoea, give morphine s.c. or as an intravenous (i.v.) infusion. Start with 0.5 mg/h and titrate. If needed, add midazolam (2.5–5 mg) or diazepam for nocturnal symptom control and to relieve anxiety (GCPP).

Enteral Nutrition in Patients with ALS

1. Bulbar dysfunction and nutritional status, including body weight, should be checked at each visit. Difficulty drinking tap water is frequently the first sign of significant dysphagia (GCPP).
2. Patients should be referred to a dietitian as soon as dysphagia appears. A speech and language therapist can give valuable advice on swallowing techniques (GCPP).
3. The timing of percutaneous endoscopic gastrostomy (PEG)/percutaneous radiologic gastrostomy (PRG) is based on an individual approach taking into account bulbar symptoms, malnutrition (weight loss of over 10%), respiratory function and the patient's general condition. Early insertion of a feeding tube is recommended (GCPP).
4. When PEG is indicated, patient and carers should be informed: (i) of the benefits and risks of the procedure; (ii) that it is possible to continue to take food orally as long as it is possible; and (iii) that deferring PEG to a late disease stage may increase the risk of the procedure (GCPP).
5. PRG is a suitable alternative to PEG. This procedure can be used as the procedure of choice or when PEG is deemed hazardous (GCPP).
6. Tubes with relatively large diameter (e.g., 18–22 Charrière) are recommended for both PEG and PRG to prevent tube obstruction (GCPP).
7. Prophylactic medication with antibiotics on the day of the operation may reduce the risk of infection (GCPP).
8. Nasogastric tube (NGT) feeding may be used in the short-term and when PEG or PRG is not suitable (GCPP).
9. Home parenteral nutrition may be used in patients with advanced ALS (GCPP).

Cognition in ALS

1. A frontotemporal syndrome occurs in up to half of patients with ALS (Level B) and is associated with a poorer prognosis. Symptoms of cognitive dysfunction may appear before or after the onset of motor symptoms.
2. The Mini-Mental State Examination is an insensitive test for ALS with cognitive impairment (ALSci) and ALS with behavioral impairment (ALSbi).
3. Rapid screening tools that include tests of verbal fluency can identify patients in whom more detailed neuropsychological evaluation is mandated (Level C).
4. In all patients with frontal dysexecutive syndromes, care needs to be taken to ensure informed consent during decision-making; capacity issues may need to be considered (GCPP).
5. Carers/healthcare professionals should be informed of the symptoms of dysexecutive syndrome and trained in their management (GCPP).

Communication in Patients with ALS

1. Regular assessment (i.e., every 3–6 months) of speech and language function by a trained speech and language therapist is recommended (GCPP).
2. Those with evidence of early language deficits should undergo full neuropsychological testing (GCPP).
3. The use of appropriate communication support systems (ranging from pointing boards with figures or words, to computerized speech synthesizers) should be individualized and appropriate training and support provided as required (GCPP).

Palliative and End-of-Life Care

1. Whenever possible, offer input from a palliative care team early in the course of the disease.
2. Initiate discussions on end-of-life decisions when the patient asks or provides an opportunity for discussion on the provision of end-of-life information and/or interventions.
3. Discuss the options for respiratory support and end-of-life issues if the patient has dyspnoea, other symptoms of hypoventilation (see Table 8 in the original guideline document) or a forced vital capacity below 50%.
4. Inform the patient of the legal situation regarding advance directives and the naming of a healthcare proxy. Offer assistance in formulating an

advance directive (GCPP).

5. Re-discuss the patient's preferences for life-sustaining treatments every 6 months (GCPP).
6. Initiate early referral to hospice or homecare teams well in advance of the terminal phase of ALS (GCPP).
7. Be aware of the importance of spiritual issues for the quality of life and treatment choices. Establish a liaison with local pastoral care workers to be able to address the needs of the patient and relatives (GCPP).
8. For the symptomatic treatment of dyspnoea and/or intractable pain, use opioids alone or in combination with benzodiazepines if anxiety is present. Titrating the dosages against the clinical symptoms will rarely if ever result in life-threatening respiratory depression (GCPP).
9. Terminal restlessness and confusion because of hypercapnia can be treated with neuroleptics (e.g., chlorpromazine 12.5 mg every 4–12 h by mouth [p.o.], i.v., or per rectum [p.r.] (GCPP).
10. Use oxygen only if symptomatic hypoxia is present (GCPP)

Definitions:

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation

Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

a. Randomization concealment
b. Primary outcome(s) is/are clearly defined
c. Exclusion/inclusion criteria are clearly defined
d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Good Clinical Practice Points (GCPP) Where there was lack of evidence but consensus was clear, the Task Force has stated its opinion as Good

Clinical Practice Points.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Clinical Practice Points (GCPP) Where there was lack of evidence but consensus was clear, the Task Force has stated its opinion as Good Clinical Practice Points.

Clinical Algorithm(s)

A flowchart for the management of respiratory dysfunction in amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND) is provided in the original guideline document.

Scope

Disease/Condition(s)

Amyotrophic lateral sclerosis (ALS)

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Rehabilitation

Treatment

Clinical Specialty

Family Practice

Gastroenterology

Internal Medicine

Medical Genetics

Neurology

Nursing

Nutrition

Physical Medicine and Rehabilitation

Psychology

Pulmonary Medicine

Speech-Language Pathology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Hospitals

Nurses

Occupational Therapists

Physical Therapists

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

Respiratory Care Practitioners

Social Workers

Speech-Language Pathologists

Guideline Objective(s)

To establish evidence-based and patient- and carer-centred guidelines for diagnosing and managing patients with amyotrophic lateral sclerosis (ALS) for clinicians

Target Population

Patients who have or who are suspected to have amyotrophic lateral sclerosis (ALS) and their carers

Interventions and Practices Considered

Diagnosis/Evaluation

1. Clinical and paraclinical examination and assessment
2. Repetition of initially equivocal tests
3. Review of diagnosis in cases without typical progression or with atypical features

Management/Treatment

1. Communicating the diagnosis and discussing the implications
2. Provision of supportive information
3. Regular appointments and contact with multidisciplinary care
4. Support for patient caregivers
5. Neuroprotective treatment with riluzole

6. Symptomatic treatment
    - Sialorrhoea: hyoscine, atropine drops or amitriptyline; botulinum toxin; irradiation of the salivary glands
    - Bronchial secretions: mucolytics; beta-receptor antagonists and a nebulizer with saline and/or an anticholinergic bronchodilator and/or a mucolytic and/or furosemide; manually assisted cough; mechanical insufflator–exsufflator; portable home suction device and a room humidifier
    - Pseudobulbar emotional lability: antidepressants; a combination of dextromethorphan and quinidine
    - Cramps: levetiracetam; physiotherapy; exercise; hydrotherapy; quinine sulfate
    - Spasticity: physical therapy; hydrotherapy; cryotherapy; oral or intrathecal antispastic drugs
    - Depression, anxiety, insomnia, fatigue: antidepressants; bupropion; benzodiazepines; hypnotics; modafinil
    - Venous thrombosis: anticoagulants; physiotherapy, limb elevation, compression stockings
7. As appropriate, counseling about cell therapies and careful record-keeping if cell therapy is pursued
8. Genetic counseling and analysis
9. Monitoring of respiratory function; non-invasive and invasive ventilation and treatment of dyspnea
10. Assessment of nutritional status; provision of nutritional support, including referral to a dietician and gastrostomy as indicated
11. Assessment of cognitive function
12. Assessment of communication difficulties by a speech and language therapist; use of appropriate communication support systems
13. Palliative and end-of-life care

Note: The following were considered but not recommended: treatment with vitamins, testosterone, antioxidants such as co-enzyme Q-10 and ginkgo biloba, intravenous immunoglobulin therapy, cyclosporin, interferons, Copaxone, KDI tripeptide, neurotrophic factors (including brain-derived neurotrophic factor [BDNF], insulin-like growth factor 1 [IGF-1] and mecasermin rinfabate), ceftriaxone, creatine, gabapentin, minocycline, stem cells or lithium; surgical intervention for sialorrhoea; prophylactic anticoagulants for venous thrombosis.

Major Outcomes Considered

- Sensitivity and specificity of diagnostic tests
- Degree of satisfaction with the communication of diagnosis
- Effectiveness of treatment (measured by, e.g., survival, number of hospital admissions and duration of hospital stay, incidence and severity of amyotrophic lateral sclerosis [ALS] symptoms, and quality of life of the patient and carers)

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Two investigators performed an independent literature search for each of 13 subjects addressed. From 2008 through February 2011, the investigators searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library to date); MEDLINE-OVID (January 1966 on); MEDLINE-ProQuest; MEDLINE-EIFL; EMBASE-OVID (January 1990 on); the Science Citation Index (ISI); the National Research Register; the Oxford Centre for Evidence-based Medicine; the American Speech Language Hearing Association (ASHA); the World Federation of Neurology ALS page of reviews of published research; the Oxford Textbook of Palliative Medicine, the UK Department of Health National Research Register (www.dh.gov.uk/en/Aboutus/Researchanddevelopment/AtoZ/DH_4002357), and national neurological databases (e.g., http://www.alsa.org , http://alsod.iop.kcl.ac.uk/). There were no constraints based on language or publication status.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Classification Scheme for a Diagnostic Measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy

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Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)

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d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Each pair of investigators prepared a written analysis that was communicated and discussed by email with the other members of the task force. A combined draft was then written by the chairman and circulated to the task force for further discussions. All recommendations had to be agreed to by all members of the task force unanimously.

The findings of the literature search were evaluated according to the recommendations of the European Federation of Neurological Societies (EFNS) resulting in level A, B or C recommendations. Where there was lack of evidence but consensus was clear, the task force has stated their opinion as Good Clinical Practice Points (GCPP) (see the "Rating Scheme for the Strength of Recommendations" field).

Rating Scheme for the Strength of the Recommendations

Rating of Recommendations for a Diagnostic Measure

Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies.

Good Clinical Practice Points (GCPP) Where there was lack of evidence but consensus was clear, the Task Force has stated its opinion as Good Clinical Practice Points.

Rating of Recommendations for a Therapeutic Intervention

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Clinical Practice Points (GCPP) Where there was lack of evidence but consensus was clear, the Task Force has stated its opinion as Good Clinical Practice Points.

Cost Analysis

- Several studies have shown that the provision of mechanical ventilation for patients causes particular strain on caregivers, reducing their quality of life and raising their responsibilities related to managing the ventilator and providing for the increasing caring costs.
- The availability and cultural acceptability of invasive mechanical ventilation (IMV) in patients with amyotrophic lateral sclerosis (ALS) varies greatly between different countries and cultures. It is costly and has significant emotional and social impacts on patients and caregivers.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see the "Availability of Companion Documents" field).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for most of the recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate clinical management of patients with amyotrophic lateral sclerosis (ALS)

Potential Harms

- In one study, fatigue was a side effect in 26% of patients taking riluzole compared with 13% receiving placebo.
- Care is needed when treating sialorrhoea (drooling or excessive salivation) in elderly patients with transdermal hyoscine (scopolamine), because of the frequent side effects of confusion or loss of bladder control.
- When treating sialorrhoea using botulinum toxin type A or type B, caution is needed in patients with significant bulbar palsy as increased dysphagia may occur, with serious consequences.
- The intravenous, intrathecal or intraparenchymal administration of haematopoietic stem cells derived from peripheral blood or bone marrow has been tested in small series of patients. Even if these procedures are safe in the short term, the studies to date have not yielded sufficiently robust data to allow translation to clinical practice. Clinical efficacy is unproven, and long-term safety still needs to be demonstrated.
- With invasive mechanical ventilation (IMV) there is a risk that some patients will develop a 'locked-in' state. IMV is costly and has significant emotional and social impacts on patients and caregivers (see Table 10 in the original guideline document for more details).
- Percutaneous endoscopic gastrostomy (PEG) requires mild sedation and is therefore more hazardous in patients with respiratory impairment and/or at an advanced stage of the disease. To minimize risks, PEG should be performed before vital capacity falls below 50% of predicted.
- Nasogastric tube (NGT) insertion can have drawbacks such as increasing oropharyngeal secretions or causing nasopharyngeal discomfort or even ulceration.

Qualifying Statements

Qualifying Statements

This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.

Implementation of the Guideline

Description of Implementation Strategy

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Safety

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis, Andersen PM, Abrahams S, Borasio GD, de Carvalho M, Chio A, Van Damme P, Hardiman O, Kollewe K, Morrison KE, Petri S, Pradat PF, Silani V, Tomik B, Wasner M, Weber M. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS) -- revised report of an EFNS task force. Eur J Neurol. 2012 Mar;19(3):360-75. [186 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

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Guideline Developer(s)

European Academy of Neurology - Medical Specialty Society

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Guideline Committee

European Federation of Neurological Societies Task Force on the Diagnosis and Management of Amyotrophic Lateral Sclerosis (MALS)

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Financial Disclosures/Conflicts of Interest

Dr. Andersen has served as a consultant for Avanir Pharmaceuticals. The other authors report no conflicts of interest.

Guideline Status

This is the current release of the guideline.

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Guideline Availability

Electronic copies: Available to registered users from the European Federation of Neurological Societies Web site .

Availability of Companion Documents

The following is available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the European Federation of Neurological Societies (EFNS) Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on December 7, 2006. The information was verified by the guideline developer on May 3, 2007.

This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on January 10, 2008, following the U.S. Food and Drug Administration advisory on Carbamazepine. This summary was updated by ECRI Institute on May 1, 2009 following the U.S. Food and Drug Administration advisory on antiepileptic drugs. This summary was updated by ECRI Institute on May 26, 2009, following the U.S. Food and Drug Administration advisory on Botox, Botox Cosmetic (Botulinum toxin Type A), and Myobloc (Botulinum toxin Type B). This summary was updated by ECRI Institute on July 20, 2009 following the U.S. Food and Drug Administration advisory on Varenicline and Bupropion. This summary was updated by ECRI Institute on August 17, 2009, following the updated FDA advisory on Botox and Botox Cosmetic (Botulinum toxin Type A), and Myobloc (Botulinum toxin Type B). This NGC summary was updated by ECRI Institute on November 20, 2012. The updated information was verified by the guideline developer on January 30, 2013. This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on Opioid pain medicines.

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